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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/583,066	05/30/2000	Erich Wanker	GPCG-P01-122	1672

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EXAMINER
MARSCHEL, ARDIN H

ART UNIT	PAPER NUMBER
1631	17

DATE MAILED: 12/31/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary

Application No.	Applicant(s)
09/583,066	Wanker et al.
Examiner	**Art Unit**
Ardin Marschel	1631

– Th MAILING DATE of this communication appears on th cov r she t with the correspondenc address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 18, 2001*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-67* is/are pending in the applica

4a) Of the above, claim(s) *60-62 and 67* is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-59 and 63-66* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-67* are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☒ The proposed drawing correction filed on *10/12/01* are a) ☒ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). (4 sheets)

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Applicants' election with traverse of Group I, specie A) protein-protein (plus protein-peptide and peptide-peptide; see discussion below regarding this specie) interaction, specie B) methods directed to identification of interacting molecules per se, and specie C) readout system also includes a counterselectable genetic element: (claims 1-59 and 63-66); in Paper No. 15, filed 10/18/01, is acknowledged. It is noted that formulation is now considered part of a non-elected specie within Group I as discussed below, but inadvertently included in specie B-2 previously. The traversal is on the ground(s) that, firstly, the Group II claims 60-62 and 67 are dependent from Group I and thus include all the limitations of Group I. Consideration of the amended claims 60-62 and new added claim 67 reveals that the methods of Group II claims do not all require the steps of the Group I claims therein. It is acknowledged that claims 60, 62, and 67 specifically require the claim 1 method steps as part of the claimed method. This is not, however, the case for claim 61. In claim 61, the identification of an inhibitor of interacting molecules is an actual method step, but said interacting molecules are cited only as being "identified by the method of claim 1". This identification is firstly a product by process limitation and secondly is cited in the claim in the past tense via the word "identified". The past tense wording indicates that said identification is performed prior to the practice of claim

61. Also, a product claimed by a process in U.S. Patent law practice includes any such product even though defined or identified by another process. Thus, claim 61, does not require the method steps of claim 1 per se in its practice. Thus, claim 61 remains in non-elected Group II. The specific inclusion of the claim 1 method steps in claims 60, 62, and 67; however; makes the pharmaceutical production a specie within the Group I claims. Since applicants' traversal arguments including the ones responded to below, are non-persuasive regarding the distinctness of said pharmaceutical production methods from methods only directed to identification of interacting molecules these claims will be treated as a non-elected specie within Group I and withdrawn from examination until such time that examination beyond the elected specie is appropriate. In case applicants wish to submit further traversal arguments regarding this specie election determination, this restriction/election requirement will not be made final at this time, but will be made final in the next office action if there are no further traversal arguments. The conditions for such extension of examination to non-elected species within a restriction group were summarized in the previous office action to which applicants are referred and are not repeated here.

Secondly, applicants argue that a search of Group I necessarily entails a search for the subject matter of Group II.

The subject matter of Group II is directed to a pharmaceutical composition formulation, thus requiring consideration and/or search for pharmaceutical practice, or inhibitor identification which are not required in the elected Group I invention. Thus, contrary to the allegations of applicants, these subject matters, of which there is clearly a massive publication base, would require and undue search burden to be searched with the elected species within Group I.

Thirdly, applicants argue that there are only four claims in Group II and that simultaneous examination of these two groups poses no significant additional burden. In response the number of claims is unrelated to subject matter therein which is the basis for these restriction and election requirements. Thus, this argument is not directed to the basis for the distinctness or the invention Groups or species.

The specie election requirements were traversed firstly regarding the species listed in claim 4 as being closely related for the following species: protein-protein, protein-peptide, and peptide-peptide. It is acknowledged that these species are closely related such that they all are hereby included within the elected specie from claim 4.

Applicants also traverse the specie election B in that inhibitors may, and frequently are, also interacting molecules of the type that would be identified in the elected specie. In

response, interacting molecules may and generally are evaluated for interaction without competition or inhibition by other molecules. Such competition or inhibition also includes consideration of relative binding affinities between different molecules. Thus, competition or inhibition consideration adds a significant and generally separate set of parameters over simple interaction determination and thus clearly is distinct subject matter requiring a separate and distinct search thus still supporting the undue search burden if interaction as well as inhibition subject matters are searched together.

Applicants then admit that they are unable to discern the rationale between positive and negative selection species. This seems not to be a traversal argument. Thus argument therefore is not directed to the basis for distinctness between species and thus moot. By way of further clarification various references will disclose selection by growth inhibition which is a negative selection but many others disclose selection by indicating a positive disclosure as to what positive content in a growth medium will result in growth without any statement as to what condition(s) will inhibit or not permit growth, albeit maybe implying that the lack of the positive growth component may result in no growth. Thus, these species are two different elements of subject matter in the way that they are disclosed as to growth conditions.

Applicants then elected a specie disclosed in Example 4.1. This election is appreciated but is not consistent with the restriction/election requirement as previously set forth and thus is non-persuasive regarding changing the specie election requirements summarized above.

The oath or declaration is defective. A new oath or declaration in compliance with 37 C.F.R. § 1.67(a) identifying this application by its Serial Number and filing date is required. See M.P.E.P. §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed alterations have been made to the oath or declaration (see 37 C.F.R. §§ 1.52(c) and 1.57). See the address alteration for Niels Wedemeyer without initials.

Claims 1-59 and 63-66 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the providing of host cells containing at least one genetic element, or protein or peptide cloned therefrom, which itself lacks an activation domain for the readout system while yet activating said readout via interaction with another appropriate genetic element, does not reasonably provide enablement for any "generic" genetic element, or protein or peptide cloned therefrom, which is capable of activating the readout system via interaction with another appropriate genetic element. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

It is noted that the instant claims lack any limitation regarding the genetic element(s) in the claims, or protein or peptide cloned therewith in the host cells of the invention, except for the positive limitation regarding activating the readout system upon interaction of the pair or complex of interacting molecules. The instant specification, however,

[redacted]

describes four important false positives as listed on page 3. Since the presence of these false positive conditions unpredictably would obscure, if not prevent, the determination of a result in the instantly claimed method; they must be considered and prevented via genetic element, host cell, and readout system limitations. None of these are present in the instant claims. Rather the genetic element as instantly claimed may vary widely as to content thus unpredictably giving a readout system indication without requiring interaction of cloned proteins or peptides that are expectedly being tested. For example, if any of the genetic elements contains activating domain(s) for the readout system, it would itself give a positive result without actual interaction of a pair or complex as desired in lines 1-2 of claim 1. It is noted that a host cell selection step (B) is set forth in claim 1 but that this step lacks any genetic element practice to prevent any of the four false positives noted above. It is also noted that the U.S. Patent 5,283,173 to Fields et al. recognizes some of these false positive conditions as summarized in column 7, lines 25-41, thus supporting this rejection as being directed to lack of predictable enablement which is also appreciated by the prior art.

Claims 1-59 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

[redacted]

which applicant regards as the invention.

In claim 1, line 5, a plurality of genetic elements is cited whereas as few as a single such element is provided in lines 3-4 thus making the single element practice of lines 3-4 conflict in number with the remainder of the claim. Clarification via clearer claim wording is requested. This unclarity is present in claims dependent directly or indirectly from claim 1 due to their dependence.

In claim 1, line 2, a pool is cited but confusingly nowhere in the claim is there recitation of usage of such a pool for the method of identification of the claim. Clarification is requested regarding the metes and bounds of the claim practice which sets out to identify molecules from a pool but then lacks any such identification in actual claim steps. This unclarity is present in claims dependent directly or indirectly from claim 1 due to their dependence.

In several claims the limitation "preferably" is present, such as at claims 17, 35-37, and 59. This causes these claims to be vague and indefinite due to a lack of determination or clarification of the conditions under which preferable selection is thereby indicated. Clarification via clearer claim wording is requested.

In claim 25, line 2, it is unclear whether the "automated" limitation is meant only for "arraying" or also to modify the

remaining limitations in the list. This unclarity is present in claims 31 and 43 also.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 2, 3, 11, 12, 55-57, 65, and 66 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Vidal et al.[PNAS 93:10315(1996)].

Vidal et al. identifies interacting molecules via the introduction of genetic elements encoding interacting proteins as depicted, for example, on page 10316 in Figure 1. Yeast host cells are utilized which are selected for reporter or readout system gene activity in the METHODS section. It is noted that the determination of mutations which disrupt protein-protein interaction is the main topic of the reference but that such disruption is detected via comparison to the detection of

positively interacting proteins thus also anticipating the instant claims. The readout system is visually toxic to the host cells as shown by growth inhibition upon activation as noted on page 10316, first paragraph of the RESULTS section which also anticipates this step in claim 3, step (B). A regular grid pattern of cells is shown on page 10317, Figure 2, as required in the last 2 lines of claim 3.

Claim 65 is rejected under 35 U.S.C. § 102(b) and (e) as being clearly anticipated by Fields et al.(P/N 5,283,173).

Fields et al. discloses the usage of host cells which are visually differentiated by the GAL4 protein which permits growth on galactose as noted in column 6, lines 53-68, which taken with the remainder of the patent which is directed to the detection of protein-protein interaction via genetic element interaction as required in the kit part (Q) of claim 65 anticipates the above instant claim.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[redacted]

> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 63-66 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fields et al.(P/N 5,283,173).

As noted above the Fields et al. disclosure describes the host cells and genetic element limitations of claim 65, but also suggests and motivates the usage of other hosts such as bacterial cells or mammalian cells as in column 8, lines 48-58.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the Fields et al. invention wherein the host cells include other motivated types such as bacterial etc. thus resulting in non-yeast embodiments of the instant claims also.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with

the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

December 28, 2001

ARDIN H. MARSCHEL
PRIMARY EXAMINER